Tocilizumab treatment in severe recurrent anti-MOG-associated optic neuritis

Hayward-Koennecke, Helen ; Reindl, Markus ; Martin, Roland ; Schippling, Sven

DOI: https://doi.org/10.1212/wnl.0000000000007312

Tocilizumab treatment in severe recurrent anti-MOG-associated optic neuritis

Helen Hayward-Koennecke, MD, Markus Reindl, MD, Roland Martin, MD, and Sven Schippling, MD

Neurology® 2019;92:765-767. doi:10.1212/WNL.0000000000007312

Correspondence
Dr. Hayward-Koennecke
helen.hayward-koennecke@usz.ch

MORE ONLINE

→ **Class of Evidence**
Criteria for rating therapeutic and diagnostic studies
NPub.org/coe

Patients presenting with a clinical phenotype indicative of neuromyelitis optica spectrum disease (NMOSD) including its limited variants such as recurrent optic neuritis (ON) or longitudinally extensive transverse myelitis negative for AQP-4 antibodies may test positive for immunoglobulin G antibodies against myelin oligodendrocyte glycoprotein (MOG), a transmembrane protein expressed on oligodendrocytes and the outer layers of the myelin sheath. MOG antibody-associated autoimmunity has gained increasing attention over recent years due to its clinical overlap with NMOSD, despite the latter being considered an autoimmune astrocytopathy. Anti-MOG antibody-positive patients show a relapsing disease course that can lead to substantial visual loss and spinal cord involvement.[1–3] Data on therapy in MOG antibody-associated disease as of yet is limited, but similar to NMOSD, it appears critical to start an efficacious treatment early in order to prevent severe functional sequelae including blindness. Tocilizumab (TCZ), a humanized antibody targeting the interleukin-6 (IL-6) receptor, has shown promise in patients with breakthrough disease and highly active forms of AQP-4 antibody-positive NMOSD.[4,5] Prolonged treatment with TCZ has been reported both efficacious and safe[5] and leading to a reduction of AQP-4 antibody titers.[4,5]

We present a case of an anti-MOG seropositive patient, who is stable on TCZ for more than 4.5 years after having failed various immunotherapies including the anti-CD20 antibody rituximab and cyclophosphamide.

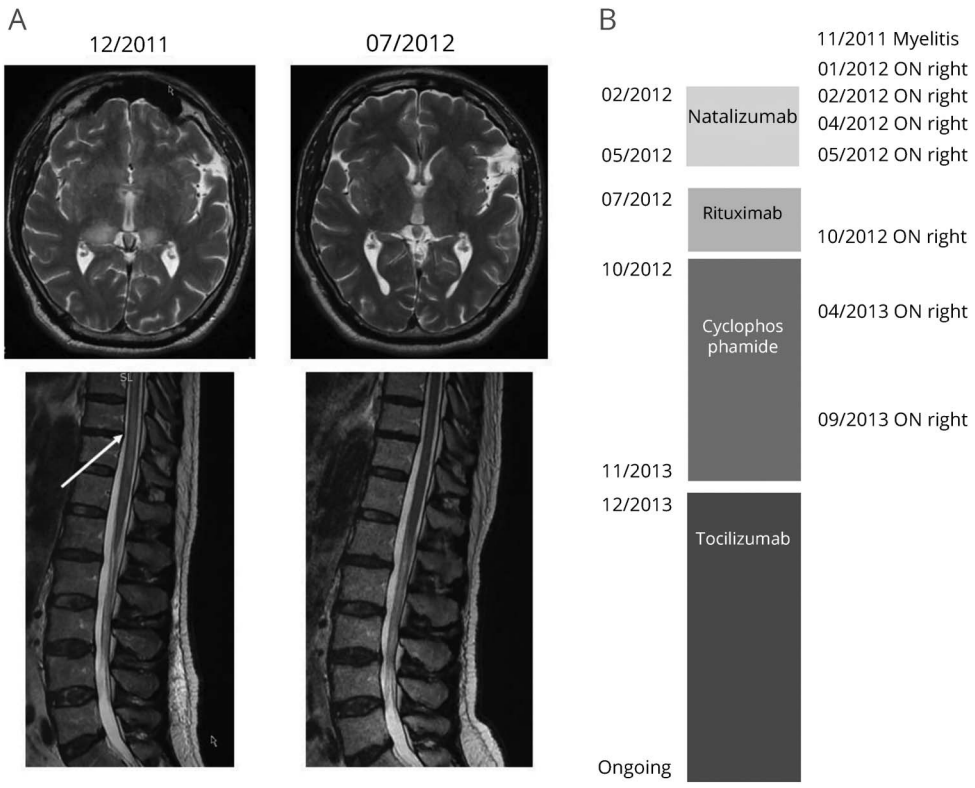
Case report

A 59-year-old man was admitted to our hospital due to gait ataxia, urinary retention, constipation, nystagmus, and double vision. The initial MRI showed multiple, nonlongitudinally extensive T2 hyperintense lesions in the cervical, thoracic, and lumbar spinal cord, as well as lesions in both thalami and the pons (figure). Short-term MRI follow-up indicated progressive hyperintense lesions in the cervical cord with gadolinium enhancement. CSF analysis revealed 15 mononuclear cells per μL and an elevated protein of 906 mg/L, whereas oligoclonal bands were negative. The patient tested negative for anti–AQP-4 antibody twice. Extensive bacteriologic and virology screenings remained unremarkable, and the patient improved on high-dose steroids. Three months later, he developed ON of the right eye followed by 6 relapses over the following 19 months while the left eye was affected once. Every relapse was treated with high-dose steroids followed by plasmapheresis once with only partial recovery leading to a residual visual acuity below 20/400 (Snellen chart) on the right. Initially, treatment with the anti-VLA4 monoclonal antibody natalizumab had been initiated (3 administrations in total) followed by rituximab (2 × 1 g in 2 weeks) due to disease breakthrough (figure). Due to further relapses, the patient was switched to cyclophosphamide (in total 12 administrations). Following further clinical and MRI breakthrough activity (relapsing ON) and suspected seronegative NMO, monthly TCZ (8 mg/kg body weight) was initiated for 12 months and then tapered to applications every 6 weeks. Meanwhile the patient tested positive for anti-MOG antibodies (titer 1:320). Currently, a bimonthly TCZ regime is implemented. No further relapses have occurred, MRI has remained stable throughout, and new lesions have not been detected.

From Neuroimmunology and MS Research, Neurology Clinic (H.H.-K., R.M., S.S.), University Zurich, Switzerland; and Clinical Department of Neurology (M.R.), Medical University of Innsbruck, Austria.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Figure MRI findings, treatment history, and relapse timeline



(A) MRI scans: left: T2-hyperintense bilateral thalamic and longitudinally extensive lumbar spinal cord lesion; right: follow-up scan 7 months later without T2-hyperintense lesions. (B) Timeline of treatment interventions. ON = optic neuritis.

Discussion

MOG antibody-associated disease can present with relapsing disease leading to severe functional deficits including severe visual impairment and spinal cord syndrome.[1–3] Efficacious immune treatment should therefore be implemented early. Currently, no treatment consensus exists for this entity. We observed natalizumab not only failing to control but worsen disease activity, which has similarly been reported for AQP-4 antibody-positive cases.[6] We suggest that, similar to AQP4 antibody-positive NMOSD, the administration of TCZ in MOG antibody-associated autoimmunity should be evaluated early as well as in cases of treatment failure to anti-CD20 therapy (rituximab).[7] Our single case report without controls provides Class IV evidence on the efficacy of the IL-6 antibody TCZ in MOG antibody-associated autoimmunity.

Study funding

No targeted funding reported.

Disclosure

H. Hayward-Koennecke has nothing to disclose. M. Reindl: The University Hospital and Medical University of Innsbruck (Austria, employer of M.R.) receives payments for antibody assays (MOG, AQP4, and other autoantibodies) and for MOG and AQP4 antibody validation experiments organized by Euroimmun (Lübeck, Germany); and is supported by research grants from the Austrian Federal Ministry of Science and Economy (grant BIG WIG MS, Markus Reindl), the Austrian Research promotion Agency (FFG, Bridge 1 project No. 853209 EDNA), the Austrian Science Fund (FWF, project W1206 SPIN), and the Austrian Multiple Sclerosis Research Society. R. Martin received financial compensation for lectures and advisory tasks from Roche. S. Schippling reports no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* July 31, 2018. Accepted in final form January 18, 2019.

Appendix Authors

Name	Location	Role	Contribution
Helen Hayward-Koennecke, MD	University Hospital Zurich, Switzerland	Author	Drafted the manuscript for intellectual content
Markus Reindl, PhD	Medical University of Innsbruck, Austria	Author	Revised the manuscript for intellectual content
Roland Martin, MD	University Hospital Zurich, Switzerland	Author	Revised the manuscript for intellectual content

Appendix *(continued)*

Name	Location	Role	Contribution
Sven Schippling, MD	University Hospital Zurich, Switzerland	Author	Revised the manuscript for intellectual content

References

1. Cobo-Calvo A, Ruiz A, Maillart E, et al. Clinical spectrum and prognostic value of CNS MOG autoimmunity in adults: the MOGADOR study. Neurology 2018;90: e1858–e1869.
2. Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients: part 2: epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. J Neuroinflammation 2016;13:280.
3. Jelcic I, Hanson JVM, Lukas S, et al. Unfavorable structural and functional outcomes in myelin oligodendrocyte glycoprotein antibody-associated optic neuritis. J Neuroophthalmol 2019;39:3–7.
4. Araki M, Matsuoka T, Miyamoto K, et al. Efficacy of the anti-IL-6 receptor antibody tocilizumab in neuromyelitis optica: a pilot study. Neurology 2014;82: 1302–1306.
5. Ringelstein M, Ayzenberg I, Harmel J, et al. Long-term therapy with Interleukin 6 receptor blockade in highly active neuromyelitis optica spectrum disorder. JAMA Neurol 2015;72:756–763.
6. Kleiter I, Hellwig K, Berthele A, et al. Failure of natalizumab to prevent relapses in neuromyelitis optica. Arch Neurol 2012;69:239–245.
7. Biotti D, Lerebours F, Bonneville F, Ciron J, Clanet M, Brassat D. Late-onset neutropenia and neurological relapse, during long-term rituximab therapy in myelin oligodendrocyte glycoprotein-antibody spectrum disorder. Mult Scler 2018;24: 1645–1647.

Disputes & Debates: Rapid online correspondence

The editors encourage comments on recent articles through Disputes & Debates:

Access an article at *Neurology.org/N* and click on "COMMENT" beneath the article header. Responses will be posted within 3 business days.

Before submitting a comment to Disputes & Debates, remember the following:

- Disputes & Debates is restricted to comments about studies published in *Neurology* within the last eight weeks
- Read previously posted comments; redundant comments will not be posted
- Your submission must be 200 words or less and have a maximum of five references; reference one must be the article on which you are commenting
- You can include a maximum of five authors (including yourself)

New AAN Practice Management Webinar Format Digs Deeper

The new format offers a live, 30- to 45-minute webinar with expert faculty followed by several shorter recorded online lectures that explore the topic in greater depth. Each topic concludes with a 30-minute live webchat for further participant Q&A. Purchase a single webinar series for $99 or purchase a 2019 Practice Management Webinar subscription for only $189—*that's less than $32 per webinar!*

2019 Webinar Series

- January 15 – Boss, MD: Managing a Better Practice
- March 12 – Understanding How You Get Paid
- May 21 – Everything You Wanted to Know About Your Patients but Were Afraid to Ask: Having Difficult Conversations with Patients from Vulnerable Populations
- August 13 – Increasing Revenue in Your Practice: Care Models, Ancillary Services, and Other Strategies
- October 1 – Using Technology for Better Practice Management of Stroke
- November 19 – Seeing the Future Clearly: How to Succeed in 2020

Learn more and register at *AAN.com/view/webinar*.